

Case Report

Primary intestinal type adenocarcinoma of the female genital tract, arisen from a tubulo-villous adenoma: Case report[☆]Steffi van Wessel^a, Helena Van Kerrebroeck^a, Valerie Van Bogaert^b, Philippe Tummers^{a,*}, Rudy Van den Broecke^a^a Department of Gynecology and Obstetrics, University Hospital Ghent, De Pintelaan 185, 9000 Gent, Belgium^b Department of Pediatrics, University Hospital Ghent, De Pintelaan 185, 9000 Gent, Belgium

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Introduction

Primary vaginal carcinoma accounts for less than 1% of all gynecological malignancies (Benedet et al., 2000). Histologically 66–80% is defined as squamous cell carcinoma, less than 10% is defined as adenocarcinoma (Benedet et al., 2000; Tjalma et al., 2001). This case report presents a 68-year-old woman with a primary adenocarcinoma of the intestinal type arising from a tubulo-villous adenoma in the female genital tract in the absence of DES-exposure. It's an extremely rare neoplasm (Willén et al., 1999) and the 6th case to be reported in literature.

Case report

A 68-year-old Caucasian woman, Gravida 5 Para 3 Abortus 2, suffered from purulent vaginal discharge. Surgical history: appendectomy. Physical examination revealed a painful and hard nodule of 1 × 1.3 cm at the posterior border of the introitus of the vagina, without signs of infection. Cervical cytology showed no evidence for intraepithelial lesion or malignancy. Transvaginal ultrasound showed a normal uterus and ovaries, no free fluid was seen in the abdomen. The vaginal nodule was excised and examined microscopically. It revealed an invasive adenocarcinoma of the intestinal type arisen from a tubulo-villous adenoma (Fig. 1). There was no evidence of lympho-vascular invasion. Immunohisto-

chemical evaluation showed strong positivity for CEA, CK20 and CK7. There was no expression of estrogen or progesterone receptors and there was no increased expression of P53. Further clinical examination, chest X-ray, mammography, colonoscopy, PET-CT and CEA level excluded the presence of an adenocarcinoma of another location. The suspicion of this lesion to be a primary vaginal adenocarcinoma of the intestinal type was confirmed. The patient underwent a partial vulvectomy. Microscopic investigation of the resection piece showed no residual tumor. The postoperative recovery was complicated by a urinary tract infection, which was treated. The patient was discussed at the multidisciplinary oncological board, which advised a close follow-up. The patient is still disease free after 25 months follow-up.

Discussion

Primary vaginal adenocarcinomas are uncommon neoplasms and can be divided into two categories. The first category is associated with in utero DES exposure, resulting in a clear cell carcinoma. In the majority of these cases patients are younger than 40 years of age (Tjalma and Colpaert, 2006). The second group is not associated with DES exposure and consists of women in their late reproductive and postmenopausal years. This group accounts for 4.7–9.6% of all vaginal carcinomas (Tjalma et al., 2001). In this case report we describe a 68-year-old woman with a primary vaginal adenocarcinoma of the intestinal type that has arisen from a tubulo-villous adenoma, without a history of DES exposure. This type of neoplasm has seldom been described in the vulva (Willén et al., 1999) and vagina (Fox et al., 1988; Yaghseizian et al., 1992) but it is well known in the gastro-intestinal tract (Lee et al., 2005). To our knowledge this is the 6th case reported in literature up to now. In comparing these 6 cases, all women were in their late reproductive or postmenopausal years. Only 2 cases report an absence of DES exposure, in all other cases this exposure is unclear (Table 1).

In the presented case the intestinal type adenocarcinoma of the vagina was arising from a tubulo-villous adenoma. These adenomas are also exceptionally rare in the vagina. To our knowledge there are only three previous reports in literature to be found.

The etiology of an adenocarcinoma of the intestinal type in the female genital tract is unclear. Several possible theories have been described: intestinal metaplasia in foci of adenosis, heterotopic intestinal tissue, cloacal remnants (Fox et al., 1988; Yaghseizian et al., 1992), mesonephric remnants (Benedet et al., 2000; Yaghseizian et al., 1992) and endometriosis (Benedet et al., 2000; Yaghseizian et al., 1992).

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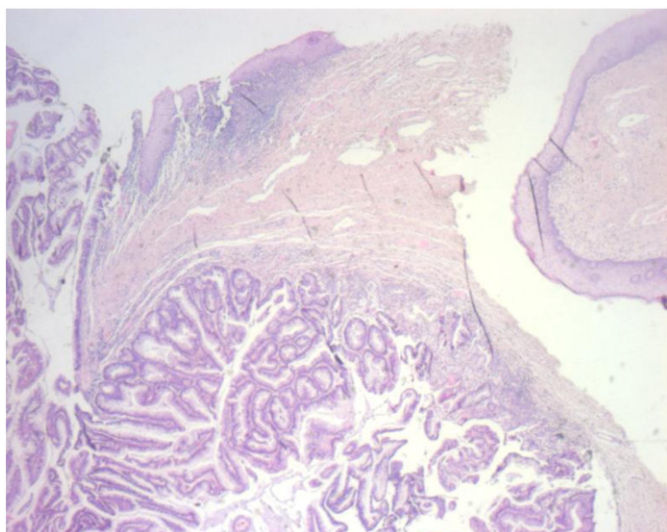


Fig. 1. Microscopic image: invasive adenocarcinoma of the intestinal type arisen from a tubulo-villous adenoma. Hematoxylin-eosin stain.

The first theory is based on the knowledge that intestinal metaplasia can arise in tissue of Mullerian origin (Fox et al., 1988). When embryological development of the Mullerian ducts is disrupted, Mullerian glandular epithelium can sequester into vaginal mucosa and adenosis arises. A well known trigger for this mechanism is the in utero DES exposure (Mudhar et al., 2001), although it has also been reported in cases without a history of DES exposure (Scurry et al., 1991).

Neoplastic transformation, the stepwise progression from metaplasia to dysplasia to carcinoma, can arise in adenosis (Mudhar et al., 2001). It is thought that the metaplasia in such a lesion arises as a response to a stressful cellular event, like the acidic vaginal environment or DES exposure (Mudhar et al., 2001). An association between adenosis and primary vaginal adenocarcinoma has been reported (Yaghsezian et al., 1992). In the presented case no adenosis was demonstrated. A second theory is the existence of heterotopic intestinal epithelium. This however has never been described (Fox et al., 1988).

The third theory is the possibility of a cloacal remnant. When areas of developing anorectal tissue are incorporated into the posterior vaginal wall during the division process of the cloaca, remnants may arise. These remnants are capable of undergoing dysplastic changes in the presence of a hostile vaginal environment (Tjalma and Colpaert, 2006). The presence of a normal intestinal type columnar epithelium adjacent to a normal squamous epithelium in the vagina has been described to progress through dysplasia to adenocarcinoma (Tjalma and Colpaert,

2006). These adenocarcinomas are thought to be of cloacogenic origin (Mudhar et al., 2001). They have been described in the vagina (Fox et al., 1988; Mortensen and Nielsen, 1991) and the vulva (Willén et al., 1999), mostly in postmenopausal women (Willén et al., 1999), although some premenopausal cases have been noticed (Fox et al., 1988; Lee et al., 2005; Mortensen and Nielsen, 1991). Both in the presented case as in the other 5 cases (Table 1), the lesion is localized at the posterior border of the introitus, which is embryologically derived from the urogenital sinus. This location allows the possibility of cloacal remnants, as described by Tjalma and Colpaert (2006).

A fourth theory is the presence of mesonephric remnants (Benedet et al., 2000; Yaghsezian et al., 1992). These are most often situated deep in the lateral walls of the vagina (Tjalma and Colpaert, 2006). The location in the presented case argues against this theory.

A fifth theory is based on the existence of endometriosis (Benedet et al., 2000; Yaghsezian et al., 1992). No clinical evidence of endometriosis was found in the presented case.

Primary vaginal adenocarcinoma of the intestinal type is extremely rare. Extensive research should be performed to exclude a primary adenocarcinoma of another location such as the rectum, colon, breast, ovary, uterus or cervix (Tjalma and Colpaert, 2006). In this case clinical examination, vaginal ultrasound, mammography, colonoscopy, chest X-ray, PET-CT and CEA level were performed. These investigations revealed no other primary adenocarcinoma. Supplementary investigations performed in other cases are examination under anesthesia, rectoscopy, sigmoidoscopy, MRI, CT, cystoscopy and gastroscopy (Willén et al., 1999; Tjalma and Colpaert, 2006; Mudhar et al., 2001). Immunohistochemical stains may be helpful in determining the origin of a tumor. In the presented case there was strong positivity for CEA, expressed in normal colon and colon carcinoma (Willén et al., 1999). Combined expression of CK7 and CK20 was found as well. In colon carcinomas, CK20 is consistently expressed (Mudhar et al., 2001).

Guidelines for treatment are not yet available because of the rare occurrence of the intestinal type adenocarcinoma of the vulva. In the presented case a partial vulvectomy was performed after a local excision of the nodule. No tumoral remnants were found, showing that the local excision had removed all tumoral tissue. In most published cases extensive surgery was performed (Table 1). Other treatment options described are (chemo)radiation, which also can be used in a neoadjuvant or adjuvant setting. Wide local excision with microscopically free resection margins of more than 1 cm seems to be the best therapeutic option with little morbidity. The disease seems not to be associated with regional or distant metastases.

There are no data in literature regarding long-term survival of this type of tumor. The longest follow-up yet reported has been 27 months (Table 1). In the presented study, the patient was free of disease after 25 months of follow-up. Close follow-up is recommended during the first 3 years because relapse was described 9 months and 23 months

Table 1

Overview of reported cases of intestinal-type adenocarcinoma of the female genital tract, arisen from a tubulo-villous adenoma.

Authors	Age	Symptomes	Location	Size	Therapy	Follow-up	Outcome	K20/K7	DES
Fox et al., 1988	59	Vaginal discharge and bleeding	Hymenal ring	2 cm	LE, silver nitrate fulguration of base	Not available	Not available	Not known	Not known
Mortensen and Nielsen, 1991	43	Vaginal discharge and contact bleeding	Posterior rim of carunculus hymenalis	1.7 × 1 × 0.9 cm	Extensive local excision and repeated re-resections	27 months	23 months: rebiopsy and re-resection showed remnants of tumor	Not known	Not known
Willén et al., 1999	57	Asymptomatic	Left posterior part of vestibulum vaginae	1 cm	Extensive local excision	26 months	No evidence of disease	Not known	Not known
Lee et al., 2005	61	Intermittent vaginal spotting	11'o clock introitus position, near the urethra	2 × 1 cm	Extensive LE and laser vaporization	9 months	9 months: recurrence at the same position, wide LE	POS/POS	Not known
Tjalma and Colpaert, 2006	55	Postmeno-pausal bleeding	Posterior and anterior in the lower vagina	4.5 × 4 × 2.7 cm	Total Infra-levator exenteration	20 months	No evidence of disease	POS/POS	No
van Wessel et al., 2013	68	Purulent vaginal discharge	Posterior introitus position	1 × 1.3 cm	LE and partial vulvectomy	25 months	No evidence of disease	POS/POS	No

after primary treatment (Table 1). The disease tends to recur locally, no locoregional or distant metastases have been reported (Lee et al., 2005; Mortensen and Nielsen, 1991). Re-excision is treatment of choice in case of recurrence (Lee et al., 2005; Mortensen and Nielsen, 1991).

Conflict of interest statement

The authors declare that there are no conflicts of interest.

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